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The Prospective Contribution of Hostility Characteristics to High Fasting Glucose Levels

The moderating role of marital status

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OBJECTIVE — To assess whether psychological constructs of hostility, anger, type A behavior pattern, and depressive symptom severity 1) were associated with concurrent and prospective fasting glucose levels and 2) whether this association was moderated by marital status.

RESEARCH DESIGN AND METHODS — Participants were 485 healthy men (mean \pm SD age 59 ± 7 years) without a history of heart disease, diabetes, or taking related medications in the Veterans Affairs Normative Aging Study. Their fasting glucose levels between 1986 and 1995 were examined. Hierarchical linear regressions were conducted to investigate whether hostility, anger, type A behavior, and depressive symptoms were associated with concurrent fasting glucose levels as well as fasting glucose 9 years later, controlling for standard sociodemographic and biomedical covariates, including baseline fasting glucose, age, education, marital status, BMI, total cholesterol, and systolic blood pressure.

RESULTS — Although none of the psychological variables were associated with concurrent fasting glucose, Cook-Medley hostility ($\beta = 0.105$), anger ($\beta = 0.091$), and type A behavior ($\beta = 0.152$) each were associated with prospective fasting glucose 9 years later, controlling for standard covariates. Depressive symptom severity was not associated with either concurrent or follow-up glucose levels. Further analysis showed that marital status moderated the effects of these characteristics on follow-up fasting glucose such that hostility, anger, and type A behavior were significant only among those who were not married ($\beta = 0.348, 0.444, 0.439$, respectively; all $P < 0.001$).

CONCLUSIONS — Hostility, anger, and type A behavior appear to be independent risk factors for impaired glucose metabolism among unmarried older men.

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Mounting evidence has demonstrated that some psychological factors are independently and prospectively associated with the incidence of type 2 diabetes and coronary artery disease (CAD). For example, depression and anger have been shown to be associated with incidence of type 2 diabetes (1,2). Hostility, anger, type A be-

havior, and depressive symptoms have also been found to predict CAD onset (3).

Impaired glucose metabolism, indicated by insulin resistance and elevated glucose levels, is well recognized as a precursor of both type 2 diabetes and CAD (4) as well as a defining feature of the metabolic syndrome (5). Hyperglycemia has also been linked to a number of patho-

physiologic processes giving rise to both type 2 diabetes and CAD, including obesity, dyslipidemia, hypertension, inflammation, and procoagulation (6). Despite its prominent role in disease development, there is a dearth of research exploring whether impaired glucose metabolism is associated with the psychosocial variables implicated in the onset of type 2 diabetes and CAD.

A few studies have investigated the association between hostility-related characteristics and glucose metabolism. In a group of 55 Japanese men, an anger-hostility scale was significantly correlated with glycosylated hemoglobin (7). In another study of 64 healthy men, hostility, type A behavior, and vital exhaustion were associated with elevated serum glucose, insulin, and insulin-to-glucose ratio, whereas anger was not (8). Vitaliano et al. (9) observed that, in a group of 150 nondiabetic elderly individuals, either a combined anger-out/hostility trait or daily hassles was associated with higher glucose after controlling for obesity, lipids, and cardiovascular disease.

Some studies found that the relationship between hostility and glucose metabolism appeared to be moderated by individual characteristics. Among women, but not men, Suarez (10) observed that anger-out and hostility were concurrently associated with fasting insulin and the homeostasis model assessment of insulin resistance, while anger-out was also correlated with fasting glucose. Similarly, in a group of 98 individuals, Surwit et al. (11) found that hostility was correlated with fasting glucose and the homeostasis model assessment index only among women or among African Americans. Siegman et al. (12) reported that impulsive anger-out was correlated with elevated fasting glucose levels in 105 healthy middle-aged women but only in those who were physically unfit. In another large-scale study, hostility was found to be associated with concurrent glucose levels in women with high familial risk for CAD but not in those with av-

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Table 1—Descriptive statistics of the participants

Age (years)	59.0 ± 7.0
Marital status (% married)	79.6
Education (% above high school education)	76.3
Ethnicity (% Caucasian)	96.7
Fasting glucose at baseline (mmol/l)	5.48 ± 0.52
Fasting glucose at follow-up (mmol/l)	5.65 ± 0.96
BMI at baseline (kg/m ²)	26.6 ± 3.2
HDL cholesterol at baseline (mmol/l)	1.30 ± 0.35
LDL cholesterol at baseline (mmol/l)	4.23 ± 0.93
Total cholesterol at baseline (mmol/l)	6.27 ± 1.05
Triglycerides at baseline (mmol/l)	1.59 ± 0.90
Systolic blood pressure at baseline (mmHg)	127.3 ± 15.0
Diastolic blood pressure at baseline (mmHg)	78.7 ± 8.1

Data are means ± SD or percent.

erage risk or in men (13). Considering that positive findings emerged only among specific groups, these studies suggest the need to examine interactions between psychological factors and sample characteristics on glucose values.

Depression is another psychological factor associated with risk of type 2 diabetes. A meta-analysis suggests a 37% increase in risk of developing type 2 diabetes among those with elevated depressive symptoms and those diagnosed with depression (1). The review also acknowledges that the underlying mechanism linking depression and diabetes is unclear. As an early indicator of type 2 diabetes, impaired glucose metabolism appears to be a plausible candidate for further examination. Nevertheless, few studies have investigated whether depression may affect glucose metabolism. One study (10) showed that elevated depressive symptoms were associated with higher insulin levels and greater insulin resistance in nondiabetic women but not in men. Some studies (16) demonstrated that individuals diagnosed with depression showed greater insulin and glucose response to glucose tolerance tests.

Despite these promising findings, some prominent limitations are noted. First, these studies were predominantly cross-sectional and merely examined concurrent associations. It is unknown whether psychological factors are associated with glucose control over time. Most prior studies were conducted with relatively small samples, thus casting some doubt in their generalizability. Furthermore, covariates of glucose measures, such as age, education, BMI, lipids, and blood pressure, were not consistently controlled across studies and might have confounded the observed relationships. In addition, marriage or spousal support,

especially for men, has long been recognized as a protective factor against health decline directly while it may also buffer the detrimental impact of other risk factors on health (14,15). It may be important to consider marriage for its direct protective effect on health promotion and its role in moderating the influence of other risk factors on health outcomes.

In attempts to address the issues raised above, this study aimed to investigate whether psychological risk variables, including hostility-related characteristics and depressive symptom severity, were associated with glucose levels either concurrently or prospectively over ~9 years. In addition, we also explored whether the purported relationship would be moderated by other individual characteristics, including age, education, and marital status.

RESEARCH DESIGN AND METHODS

Participants were from the Normative Aging Study, a longitudinal study designed to investigate biomedical and psychosocial changes associated with aging. The study recruited men from the Boston area who were healthy and without a history of chronic illnesses at entry. All participants provided written informed consent. The sampling and design of the study have been reported in detail previously (17).

To be included in this study, participants were required to 1) have completed the Minnesota Multiphasic Personality Inventory (MMPI) in 1986 and 2) have provided a fasting blood sample around 1986 and another one ~9 years later. Participants were excluded if they had a history of CAD (angina pectoris, ischemic heart disease, and myocardial infarction) or diabetes at baseline.

There were 692 participants at base-

line, among whom 207 did not provide blood samples at follow-up and were excluded. The excluded participants did not differ from those with follow-up glucose in BMI, cholesterol, and all psychological variables except that they tended to be older (aged 63.0 ± 8.5 vs. 59.0 ± 6.9 years, $t [690] = 6.58$; $P < 0.01$), more likely to be unmarried (30 vs. 20%, $\chi^2 [1] = 7.40$; $P < 0.01$), and had slightly higher systolic blood pressure (130 ± 16 vs. 127 ± 15 mmHg, $t [690] = 2.48$; $P < 0.05$).

The descriptive statistics of the final sample of 485 men are shown in Table 1. They were predominantly Caucasian between 42 and 76 years of age with a mean of 59.0 ± 7.0 years. The majority were married and had at least a high school education. On average, they consumed 1.5 ± 2.0 alcoholic drinks and smoked 1.1 ± 1.5 cigarettes per day.

Participants represented a fairly healthy population of older men at baseline, with normal average HDL cholesterol, triglycerides, and diastolic blood pressure, while their average BMI, LDL cholesterol, total cholesterol, and systolic blood pressure were somewhat elevated by the current standards. Their average fasting glucose levels were within normal range (5.5 ± 0.5 mmol/l) at baseline, with 64 (13.2%) showing impaired fasting levels (between 6.11 and 6.99 mmol/l). At follow-up, fasting glucose values (5.6 ± 1.0 mmol/l) became slightly higher and more variable. There were 40 (8.2%) incidents of type 2 diabetes (fasting glucose ≥ 6.9 mmol/l) and 47 new cases of impaired fasting glucose (between 5.6 and 6.9 mmol/l) at follow-up.

After 1986, participants received medical examinations every 3 years. On the night before examination, participants were asked to refrain from eating or drinking after midnight. The examination included an update of medical history, assessment of blood pressure and anthropometric measures, and collection of a fasting blood sample.

Participants completed standard questionnaires to provide demographic background as well as information on cigarette smoking and alcohol consumption. In 1986, active participants received the MMPI form-AX by mail, from which various psychological measures were derived.

Psychological measures

Type A behavior, anger, and hostility have long been a research focus in the influence

of negative emotionality on physical health. Although hostility or anger has been suggested as the active ingredient in type A behavior, each has shown distinctive predictability of disease status in different studies (e.g., type A behavior in Kawachi et al. [18]). To understand whether these three factors represent either a separate or a common construct in predicting change in glucose levels, we examined their effects separately and in combination.

Type A behavior. The 19-item MMPI-2 Type A Scale assesses an individual's sense of time urgency, competitive attitude, impatience, and irritability. Type A individuals are recognized as fast pacing, hard driving, and highly involved at work. They are also impatient, direct, confrontational, argumentative, and short tempered during interpersonal transactions. The Type A Behavior Scale was developed to be conceptually distinct from cynical hostility during the restandardization of MMPI (19). The scale evidenced high 9-day test-retest ($r = 0.82$) and internal consistency (Cronbach's $\alpha = 0.72$) reliability (19). Its predictive validity has been established by its independent and prospective association with CAD onset (18).

Cook-Medley hostility. Hostility was assessed by the Cook-Medley Hostility Scale. It consists of 50 true-or-false items, tapping the disposition characterized by cynical attitudes, misanthropic beliefs, and aggressive responding style. Individuals with high scores tend to be suspicious and distrustful of people, perceive their environment as threatening, and see others as harboring harmful intent. The instrument has established reliability, convergent validity, and discriminant validity (20) and is associated with detrimental health habits, adverse health outcomes, and incidence of coronary disease (21).

Anger. Anger was measured with the 16-item MMPI-2 Anger Content Scale that assesses excessive anger expression and inability to control outbursts (19). Individuals with higher scores are impulsive, testy, easily annoyed, and likely to engage in physical and verbal confrontations. When provoked, they are likely to become verbally or physically aggressive and engage in swearing and fighting. The scale has high 9-day test-retest reliability ($r = 0.85$) and internal consistency ($\alpha = 0.76$).

Overall hostility factor. Considering the high correlations among hostility, an-

ger, and type A behavior ($r = 0.64$ – 0.73), we conducted a principal components analysis and extracted a single component explaining 79% of the total variance. A factor score was derived to represent an overall index for hostility, anger, and type A tendencies.

Depression symptom severity. Depressive symptom severity was assessed with the 33-item MMPI-2 Depression Content Scale (19). It assesses affective, cognitive, and behavioral symptoms of depression, including dysphoric mood, lack of interest, low motivation, feelings of guilt and worthlessness, and thoughts of suicide. The scale evidenced high 9-day test-retest reliability ($r = 0.87$) and internal consistency ($\alpha = 0.85$) (19).

Blood pressure and BMI

Blood pressure. Blood pressure was measured to the nearest 2 mmHg with a standard mercury sphygmomanometer. Systolic and diastolic blood pressure was obtained from both arms in a sitting position. An average reading from both arms was calculated for analysis.

BMI. Height was measured to the nearest 0.1 inch, and weight was measured to the nearest 0.5 lb, with the participant standing in bare feet and in undershorts. BMI was calculated from dividing weight in kilograms by the square of height in meters.

Blood chemistry assays

Fasting blood samples were obtained at 8:00 A.M. Values of glucose and cholesterol were obtained using standardized procedures (18). Serum glucose was measured in duplicate on an autoanalyzer using the hexokinase method. Serum cholesterol was analyzed with enzymatic method (SCALVO Diagnostics, Wayne, NJ). After precipitation of LDL cholesterol and VLDL fractions, HDL cholesterol was measured in supernatant with the Abbott Biochromatic Analyzer 100 (Abbott Laboratories, South Pasadena, CA). LDL cholesterol was estimated with the Friedewald method.

Data analysis

Before analysis, variables were inspected for normality. Fasting glucose values were transformed with a natural log function because of nonnormality. All psychological measures were transformed to Z scores to facilitate interpretation.

Statistical control variables

A number of sociodemographic and biomedical variables may confound the rela-

tionships between psychological variables and glucose levels. We included the following covariates in analyses as standard control variables: age, education, marital status, BMI, total cholesterol, and systolic blood pressure.

Main analyses

Hierarchical multiple regression analysis was conducted to examine the associations between psychological variables (hostility, anger, type A behavior, and depressive symptom severity) and fasting glucose levels. Each psychological variable was tested separately for its contribution to either concurrent or follow-up glucose levels. All models were controlled for standard sociodemographic and biomedical variables. In the analyses of follow-up glucose levels, baseline glucose levels were also controlled.

Additional moderation analyses

Additional analyses were conducted to investigate whether age, education, and marital status moderated the relationship between a psychological factor and fasting glucose values. Moderation of personality by demographic characteristics could either enhance or buffer their effects on glucose. Procedures described by Cohen et al. (22) were used to test interactions in regression models. In short, to test a particular interaction (e.g., anger \times marital status), we computed an appropriate interaction term by multiplying the corresponding psychological factor (e.g., anger) and sociodemographic variable (e.g., marital status) and then entered it in the regression model with all control variables and independent variables involved in the interaction. Continuous variables were centered at the mean before the interactions were calculated.

RESULTS — The correlations between psychological variables and fasting glucose levels at baseline and follow-up are presented in online appendix Table 1A (available at <http://dx.doi.org/10.2337/dc07-1945>).

Associations between psychological variables and concurrent fasting glucose values

None of the psychological variables were found to be associated with concurrent fasting glucose levels at the baseline in regression models with standard covariates ($\beta = 0.017$ – 0.050 , all $P > 0.05$).

Table 2—Unstandardized and standardized multiple regression coefficients of psychological variables in predicting follow-up fasting glucose levels* controlling for age, education, marital status, baseline glucose, BMI, total cholesterol, and systolic blood pressure

Psychological predictors	Multiple regression coefficients		
	All participants	Unmarried	Married
Cook-Medley hostility	0.016 ± 0.007; 0.105†	0.053 ± 0.014; 0.348‡	0.007 ± 0.007; 0.078
Anger	0.014 ± 0.007; 0.091†	0.067 ± 0.016; 0.444‡	0.004 ± 0.007; 0.060
Type A	0.020 ± 0.006; 0.152§	0.065 ± 0.015; 0.439‡	0.011 ± 0.007; 0.106
Overall hostility factor	0.018 ± 0.006; 0.124§	0.067 ± 0.015; 0.453‡	0.008 ± 0.007; 0.093
Depression	0.001 ± 0.007; 0.004	0.012 ± 0.013; 0.081	−0.003 ± 0.007; −0.007

Data are B ± SE; β . *Fasting glucose was transformed with a natural log function. † $P < 0.05$; ‡ $P < 0.001$; § $P < 0.01$.

Associations between psychological variables and fasting glucose values at follow-up

After controlling for baseline glucose values, age, education, marital status, BMI, total cholesterol, and systolic blood pressure, Cook-Medley hostility ($\beta = 0.105$, $P = 0.021$; model $R^2 = 0.158$, $F [9,484] = 9.884$, $P < 0.001$), anger ($\beta = 0.091$, $P = 0.036$; model $R^2 = 0.164$, $F [9,484] = 10.368$, $P < 0.001$), type A behavior ($\beta = 0.152$, $P = 0.002$; model $R^2 = 0.169$, $F [9,484] = 10.696$, $P < 0.001$), and overall hostility factor ($\beta = 0.124$, $P = 0.005$; model $R^2 = 0.170$, $F [9,484] = 10.837$, $P < 0.001$) each were found to predict fasting glucose at the follow-up. In contrast, depressive symptom severity ($\beta = 0.004$, $P = 0.929$; model $R^2 = 0.135$, $F [9,484] = 8.209$, $P < 0.001$) was not a significant predictor of follow-up fasting glucose. The R^2 and change in R^2 in each step of the regression models are presented in online appendix Table 2A. In addition to psychological variables, being unmarried ($\beta = 0.114$ – 0.121 , $P = 0.005$ – 0.008), BMI ($\beta = 0.124$ – 0.147 , $P = 0.001$ – 0.009), and baseline glucose ($\beta = 0.292$ – 0.294 , $P = 0.000$) were also significant predictors of higher fasting glucose at follow-up in various models.

To illustrate the effect of hostility factor on glucose change, we calculated the mean increase in fasting glucose of participants in each quartile of the overall hostility factor. They were 0.02, 0.03, 0.23, and 0.36 mmol/l from the lowest to highest quartile, respectively, indicating greater increases in groups with higher overall hostility ($F [3,481] = 3.68$, $P = 0.012$). We also compared those who developed new incidents of type 2 diabetes ($n = 40$) and impaired fasting glucose ($n = 47$) with those who remained healthy at follow-up. The former evidenced significantly higher anger ($t [483] = -1.99$, $P = 0.047$), type A behavior ($t [483] = -3.02$, $P = 0.003$), Cook-

Medley hostility ($t [483] = -2.20$, $P = 0.028$), and overall hostility ($t [483] = -2.71$, $P = 0.007$) scores and were more likely to be unmarried (34.5 vs. 17.3%, $\chi^2 = 12.92$, $P < 0.001$) at baseline. These two groups, however, did not differ in depressive symptom severity ($t [483] = -0.441$, $P = 0.660$). After controlling for baseline glucose and BMI, the group differences remained significant for overall hostility ($P = 0.035$) and type A behavior ($P = 0.011$), while the significance was attenuated for anger ($P = 0.098$) and Cook-Medley hostility ($P = 0.120$).

Moderations of marital status, age, and education

Marital status was found to moderate the effects of Cook-Medley hostility, anger, type A behavior, and the overall hostility factor on follow-up glucose levels. These psychological variables were significantly associated with higher fasting glucose at follow-up among unmarried men ($\beta = 0.348$, 0.444, 0.439, and 0.453, respectively; all $P < 0.001$) but not in those who were married ($\beta = 0.078$, 0.060, 0.106, 0.093, respectively; all $P > 0.05$). Neither age nor education was found to moderate the effects of psychological variables on the follow-up glucose values. Finally, further controlling for cigarette smoking and alcohol consumption per day among participants with valid smoking and drinking data ($n = 446$) did not alter the results.

CONCLUSIONS— This study demonstrated that anger, hostility, and type A characteristics, but not depressive symptom severity, independently and significantly predicted higher fasting glucose levels among older men over 9 years after controlling for baseline glucose, age, education, BMI, cholesterol, and blood pressure. This relationship was moderated by marital status such that the hostility-related characteristics predicted higher follow-up fasting glucose only for

men who were not married. Several strengths of the study bolstered the validity of the findings, including a longitudinal design, stringent statistical controls, and a relatively large sample size. Results suggest that hostility-related psychological qualities may confer higher prospective risk for impaired glucose metabolism.

Several previous studies showed that hostility, anger, and type A behavior were cross-sectionally correlated with higher fasting glucose (7–11). Although hostility-related characteristics were not correlated with concurrent fasting glucose in this study, they, in combination with marital status, predicted higher fasting glucose ~9 years later. Several reasons may explain this discrepancy. First, as prior studies compared sex differences, they demonstrated that the link between personality risk factors and indexes of glucose metabolism was seen among women but not men (10,11,13). The lack of cross-sectional findings in our sample of older men appeared to be consistent with the literature. Second, this study applied stringent statistical control for covariates, which may have attenuated the relationship between psychological factors and glucose levels. Third, past studies were mostly based on smaller samples that might have produced less reliable observations. Our findings suggest that although the effects of hostility, anger, and type A behavior may not be immediate, their influences on glucose metabolism can be seen cumulatively over time and shape the course of illness onset in a gradual and progressive manner.

Instead of investigating only one psychological factor as in most prior studies, we examined hostility, anger, and type A behavior either separately or in combination. The type A scale in the study was developed to be differentiated from cynical hostility or anger while focusing on behavioral signs of time urgency, impatience, and confrontational attitudes. Re-

sults indicated that their effects are similar and overlapping, suggesting that they reflect a common underlying psychological construct affecting glucose metabolism.

Several mechanisms may explain the adverse effects of hostility-related characteristics on glucose metabolism. Individuals with high hostility, anger, and type A characteristics may perceive their environment as threatening and experience heightened stress and hassles. Elevated stress may in turn induce maladaptive psychophysiological responses that adversely affect hypothalamic–pituitary–adrenal axis activation and sympathetic arousal. Prolonged hypothalamic–pituitary–adrenal activation is accompanied by elevated adrenocorticotrophic hormone, cortisol, and catecholamines that may disturb glucose metabolism and increase insulin resistance (11). This hypothesis has been supported by studies in which hostile individuals showed heightened sympathetic arousal, cardiovascular reactivity, and neuroendocrine response when facing laboratory stressors (23). Furthermore, a maladaptive stress response may increase chronic inflammation, which is implicated in impaired glucose metabolism (24). An increased inflammatory response, therefore, may be another promising mechanism linking hostility characteristics and impaired glucose metabolism.

It is noteworthy that being married had a main effect such that it was generally associated with lower fasting glucose at follow-up. Marriage also interacted with hostility factors to buffer their detrimental effects on subsequent increase in fasting glucose. The salutary health benefits of marriage have been well documented. Marriage is a primary source of support for men (14) and may help ameliorate the impact of stress and protect against excessive neurohormonal arousal (25). Unmarried men may also be less likely to monitor their health and more likely to engage in unhealthy habits such as overeating and smoking (14), thus rendering them at higher risk for illness. We speculate that married men benefited from their spouses, who helped them maintain a healthier lifestyle and curtail detrimental habits.

In addition, marriage appeared to be particularly beneficial for individuals with high hostility characteristics by counteracting their negative impact on fasting glucose. Although hostile individuals were more likely to experience higher distress and engage in unhealthy behav-

iors, their spouses may counteract these damaging effects by providing instrumental and emotional support, alleviating distress, and curtailing high-risk behaviors (26).

In contrast to past studies, we did not find that depressive symptom severity was related to concurrent or prospective fasting glucose levels. First, our study sample consisted of healthy men, whereas the majority of past studies examined individuals with diabetes (27). Depressive symptoms may bear a stronger relationship with poor glycemic control among those with diabetes than in a healthy population. Moreover, previous studies primarily observed a cross-sectional relationship, while none associated depression with change in glucose levels over time (28). Another reason may lie in the depression instrument used in the study, which predominantly assesses affective and cognitive, but not somatic, symptoms of depression. Intriguingly, some studies do suggest that depression is a risk factor for diabetes incidence (1). In light of our findings, it would be interesting to examine whether depression remains a significant predictor of diabetes onset even after controlling for hostility, anger, and type A behavior.

There are a few limitations that may also point to directions for future research. First, the sample consisted of relatively healthy and predominantly older Caucasian men without major illness, which may limit the generalizability of findings to other populations. Considering the differences in risk of type 2 diabetes across specific populations and observations of group-specific relationship between psychological factors and glucose levels (11), future research is needed to examine whether these results can be replicated among diverse samples, such as younger or older individuals, ethnic minorities, women, or those with chronic disease. Second, the assessment of marital status was limited. It was measured at baseline and a crude indicator of various aspects of marital quality. Future studies should document change in marital status over time and the different facets of marital quality in order to discern their exact influences on health outcomes. Third, diagnosis of depression was not assessed. Results, therefore, may not be extrapolated to those who are clinically depressed. Finally, we speculate that a number of stress-induced neuroendocrine and inflammatory responses may mediate the link between

psychological factors and glucose metabolism. Future research should investigate these elements in glycemic control.

In summary, this study demonstrated that hostility-related psychological characteristics are associated with increased fasting blood glucose levels among unmarried older men over ~9 years. It suggests that glucose metabolism may be a legitimate mediating mechanism explaining the link between hostility and diabetes-related illnesses. It also underlines the importance of identifying a psychosocial profile of older men at higher risk for impaired glucose metabolism.

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